REMARKS

Claims 1-8, 24-35, 38, 40-54 and 56 will be pending upon entry of the above-made amendments. Claims 28-33 and 40-46 have been withdrawn from consideration as being drawn to a non-elected invention.[1] Applicants gratefully acknowledge the Examiner's indication that claims 4 and 5 are merely objected to and are deemed to be allowable over the art of record.

Applicants thank the Examiner for the courtesy of participating in a telephonic interview on October 25, 2005 to discuss claim 24 directed to pharmaceutical compositions and to generally discuss the withdrawn method claims.

In accordance with the claim language agreed upon during the telephonic interview and as set forth in the Interview Summary mailed October 31, 2005 in connection with the above-identified application, claim 24 has been amended to recite that the pharmaceutical composition contains a pharmaceutically acceptable carrier or a pharmaceutically acceptable diluent and a dispersing agent, a surface active agent, a binder or a lubricant. Support for this amendment is found in the present specification at least at page 23, lines 4-6. In addition, new claim 56 directed to a solid pharmaceutical composition selected from a pill, capsule or tablet has been added. Support for new claim 56 is found in the present specification at least at page 23, lines 4-6.

Claim 55 has been canceled without prejudice.

No new matter has been added.

Applicants reserve their right to prosecute the subject matter of any canceled claim, any amended claim, any withdrawn claim or any other unclaimed subject matter in one or more divisional, continuation or continuation-in-part applications.

I. Double Patenting

Claims 1-3, 6-8, 25, 27, 34, 35, 38 and 47-53 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over copending U.S. application No. 10/395,810 (the "'810 application"). Upon entry of the presently made amendments, Applicants believe that the provisional obviousness-type double patenting rejection will be the only rejection remaining in this application. Accordingly, per M.P.E.P. § 804(I)(B), Applicants respectfully submit that the

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[1] Applicants have not yet elected to cancel the unelected subject matter in anticipation of possible rejoinder.

double patenting rejection over the '810 application should be withdrawn and the present application should be allowed to proceed to issue. Applicants will then consider filing a terminal disclaimer in connection with the '810 application.

II. The Rejection Under 35 U.S.C. § 102(b)

Claims 24 and 55 have been rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by U.S. Patent No. 4,202,827 to Tzikas *et al.* ("Tzikas"). In particular, the Examiner has alleged that Example 12 of Tzikas anticipates claims 24 and 55 of the present application because Tzikas discloses water which useful as a liquid carrier and, accordingly, all of the claim limitations have been met.

Without acquiescing in the rejection, claim 24 has been amended to recite that the pharmaceutical composition contains a pharmaceutically acceptable carrier or a pharmaceutically acceptable diluent and a dispersing agent, a surface active agent, a binder or a lubricant. Claim 55 has been canceled without prejudice.

Accordingly, in view of the above remarks and amendment, Applicants respectfully submit that the rejection of claims 24 and 55 under 35 U.S.C. § 102(b) has been overcome and must be withdrawn.

III. The Rejection Under 35 U.S.C. § 103(a)

Claims 3, 26, 27, 52 and 54 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over U.S. Patent No. 4,556,654 to Showalter *et al.* ("Showalter"). In particular, the Examiner has alleged that structure-activity relationship data as a whole would not discourage one of ordinary skill in the art from selecting a subgenus wherein Z is H (*i.e.*, N-2 unsubstituted compounds) and has invited Applicants to submit side-by-side data showing unexpected, beneficial and superior results.

The Examiner has pointed to *In re Lemin* for the proposition that the indiscriminate selection of "some" among "many" is *prima facie* obvious. *In re Lemin*, 332 F.2d 839 (1964). Applicants note that the U.S. Court of Customs and Appeals reversed an obviousness rejection to claims reciting compounds within a prior art genus when Lemin demonstrated unexpected activity of the claimed subgenus. *Id.* at 841.

Applicants submit herewith a peer-reviewed literature publication (Bennett *et al.*, "SPC600125, an anthrapyrazolone inhibitor of Jun N-terminal kinase," *PNAS 98(24)*"13681-13686 (2001)) which sets forth comparative data demonstrating unexpected and superior biological activity of N-2 unsubstituted compounds relative to N-2 substituted compounds

(*see* page 13682, Fig. 1). In particular, the data demonstrates that the N-2 unsubstituted compounds (*i.e.*, SP600125, Compound D and Compound E) have superior JNK inhibitory activity relative to N-2 substituted compounds (*i.e.*, Compounds A-C). This reference also discusses the importance of the free NH group in the pyrazoloanthrone core structure of the presently claimed compounds (*see* page 13683, first full paragraph). Applicants respectfully submit that the data rebuts even a *prima facie* case of obviousness over Showalter. *In re Chupp*, 816 F.2d 643, 646 (Fed. Cir. 1987). An illustrative JNK assay protocol is set forth in the specification as filed as Example 8 at page 50.

Accordingly, Applicants respectfully submit that the rejection of claims 3, 26, 27, 52 and 54 under 35 U.S.C. § 103(a) cannot stand and must be withdrawn.

IV. Objection to claims 4 and 5

The Examiner has acknowledged that claims 4 and 5 are allowed over the art of record, but claims 4 and 5 remain objected to, presumably as being dependent upon a rejected base claim. Applicants respectfully submit that all presently pending claims are in condition for allowance in view of the above amendments and remarks and that the objection to claims 4 and 5 must be withdrawn.

V. Withdrawn Claims

Method claims 28-33 and 40-46 are currently withdrawn from consideration. In the telephonic interview of October 25, 2005, the Examiner indicated that rejoinder of method claims would be considered and suggested that Applicants provide references teaching a nexus between the biological activity of claimed compounds and the treatment of claimed diseases.

Accordingly, Applicants submit the following references herewith:

(1) Bennett, *et al.*, *P.N.A.S. 98(24)*:13681-13686 (2001): teaches that the JNK pathway is involved in, *inter alia*, diseases including arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease, graft vs. host disease, stroke, Parkinson's disease, ischemia/reperfusion injury, and myocardial infarction, (see page 13681, end of first full paragraph after the abstract);

(2) Haunstetter, *et al.*, *Circ. Res. 82*:1111-1129 (1998): teaches that the JNK pathway is involved in apoptosis (see page 1119, second column, lines 21-22) which is critically involved in cardiovascular diseases, including atherosclerosis (see page 1120, second column, first paragraph of section 8 and Table 4);

(3) Kim, *et al.*, *J. Pharmacol. Sci. 91*:177-181 (2003): teaches that the JNK pathway is involved in cardiovascular disease and restenosis following angioplasty (see page 180, Conclusions and future directions),

(4) Izumi, *et al.*, *Hypertension 36*:511-516 (2000): teaches that JNK is involved in cardiac hypertrophy (see page 511, last sentence of Abstract);

(5) Reimold, A.M., *Current Drug Targets - Inflammation & Allergy 1*:377-395 (2002): teaches that TNFα is implicated in diseases such as rheumatoid arthritis, Crohn's disease, spondylitis, ulcerative colitis and psoriasis (see Table 2 at page 385), and that controlling MAP (*e.g.*, JNK) kinase activity is a possible avenue for regulating TNFα (see end of second column at page 387);

(6) Downey, *et al.*, *Frontiers in Bioscience 3*:468-476 (1998): teaches that the JNK pathway is involved in multiple organ failure and septic/endotoxin shock (see page 468, Abstract and page 472, Miscellaneous Effects of LPS);

(7) Rückle, *et al.*, *J. Med. Chem. 47*:6921-6934 (2004): teaches that the JNK pathway is involved in *inter alia* neurodegenerative diseases, epilepsy, irritable bowel syndrome, multiple sclerosis and rheumatoid arthritis (see Abstract and page 6921, second column, first full paragraph);

(8) Hassan, *et al.*, *Virology 333*:324-336 (2005): teaches that the JNK pathway is involved in hepatitus C virus infection (see Abstract and summary on page 333, first column, first full paragraph);

(9) Nath, *et al.*, *European Journal of Pharmacology 506*:273-283 (2005): teaches that the JNK pathway is involved in bronchial hyperresponsiveness and asthma (see Abstract and summary on page 282, last paragraph);

(10) Atzori, *et al.*, *Journal of Neuropathology 60(12)*:1190-1197 (2001): teaches that the JNK pathway is associated with hyperphosphorylated tau, which is associated with neurodegenerative diseases such as Alzheimer's disease (see Abstract and first paragraph of Introduction);

(11) Middlemas, *et al.*, *Brain 126*:1671-1682 (2003): provides support that the JNK pathway is associated with peripheral neuropathy (see Abstract and first paragraph of Introduction);

(12) Luo, *et al.*, *J. of Biol. Chem. 273(6)*:3756-3764 (1998): provides support that the JNK pathway is associated with neurodegenerative diseases such as Huntington's disease (see Abstract and summary on page 3764, last paragraph); and

(13) Manning and Davis, *Nature 2*:554-565 (2003): a review article which discusses evidence supporting the application of JNK inhibitors in inflammatory, vascular, neurodegenerative, metabolic and oncological diseases (*see* last sentence of Abstract), including rheumatoid arthritis, multiple sclerosis, asthma, inflammatory bowel disease, psoriasis and transplant rejection (*see* page 555, "Inflammatory diseases").

Applicants note that the references by Bennett, Rückle, Hassan and Manning each specifically point to SPC600125, which is the compound of pharmaceutical composition claims 24 and 58, as an illustrative JNK inhibitor.

In view of the references discussed above which document the nexus between JNK activity and claimed diseases, Applicants respectfully submit that, upon rejoinder, method claims 28-33 and 40-46 will be in condition for allowance.

VI. Conclusion

Applicants respectfully submit that all of the pending claims are now in condition for allowance. If the Examiner still disagrees, she is invited to call the undersigned to schedule an interview to resolve any remaining concerns.

It is believed that no fee is due in connection with this Reply other than that for the extension of time; however, in the event any additional fee is required, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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Date January 20, 2006

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